

# An Unusual Case of Biliary Cystadenoma

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## Abstract

Biliary cystadenomas (BCAs) are rare, benign, tumors associated with liver parenchyma, and infrequently, the extrahepatic bile ducts. There is potential for malignant transformation, and as such, complete resection is crucial. Removal of the cystic lesion helps differentiate it from other hepatic lesions, such as its malignant counterpart, biliary cystadenocarcinomas (BCACs). We present the case of a 47-year-old female with a recurrence of BCA and a review of the literature. The case outlines an unusual presentation of BCA.

**Keywords:** Biliary cystadenoma; Liver; Cyst; Ovarian-type stroma

## Introduction

Biliary cystadenomas (BCAs) are rare tumors with an incidence of less than 5% of all hepatic cystic lesions [1, 2]. They are benign hepatic neoplasms with some malignant potential [3] and are often mistaken for simple hepatic cysts. The majority present asymptotically and patients often complain of vague abdominal symptoms [4-7]. Current macroscopic criteria and imaging modalities such as ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI), have yet to clearly extrapolate the difference between BCA and biliary cystadenocarcinoma (BCAC) [8]. Complete resection is important to mitigate risk of malignant degeneration, and to help differentiate between BCA and BCAC from other benign cysts. Overall, prognosis and the chance of recurrence are favorable after complete resection.

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Here we present the case of a patient with recurrence of BCA in the gallbladder fossa.

## Case Report

### Investigations

A 47-year-old female presented to our clinic with the chief complaint of severe right upper quadrant (RUQ) pain for one month. She complained of cough, vomiting, and headaches during this time. She was 13 years status post laparoscopic cholecystectomy which was not believed to be relevant to her presentation. Physical examination showed the previous surgery's scars but was otherwise unremarkable.

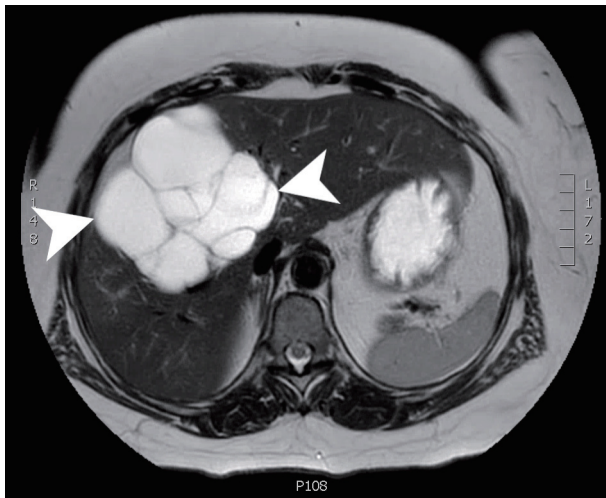
### Diagnosis

A biloma was found on CT and MRI scans. Endoscopic retrograde cholangiopancreatography (ERCP) showed a possible bile leak from the right hepatic duct and a sphincterotomy was performed. A 10-French stent was placed in the common bile duct. Endoscopic US showed no pathology, but drainage continued after stent placement. Labs were within normal limits.

The drain continued to have an output and therefore an MRI and magnetic resonance cholangiopancreatography (MRCP) was obtained. This showed a 1.9-cm mildly complex cystic lesion posterior to the drainage catheter in the gallbladder fossa. There was also mild intrahepatic biliary ductal dilation and borderline extrahepatic biliary ductal dilation with slight wall thickening.

Over the course of the next 8 months the patient continued to have persistent abdominal pain and serous output from the drain despite multiple drain studies proving inconclusive. Nine months status post ERCP an infection was discovered showing cultures that came back positive for *Pseudomonas*, *Serratia*, and *Acinetobacter* in drain fluid. She was started on trimethoprim-sulfamethoxazole (10 days) and levofloxacin (14 days) and her drain was replaced.

The patient returned for her RUQ pain with dyspepsia, nausea, and vomiting. US at that time also noted a large multilocular fluid collection in the region of the gallbladder fossa with septations and debris. Repeat imaging with MRI showed an increase in size to 10.4 × 10.2 × 14.1 cm of the multilocular cystic process involving the right lobe of the liver and gallblad-



**Figure 1.** An axial slice from a T2 weighted MRI with gadolinium contrast showing a complex, multilocular cystic mass (arrow heads) measuring  $10.4 \times 10.2 \times 14.1$  cm involving segments 8, 5 and 4B. MRI: magnetic resonance imaging.

der fossa (Fig. 1). Differential diagnosis at that time included a complex cyst, BCA/cystadenocarcinoma, complex biloma, or a possible lymphangioma. She was seen by surgery at this time. The patient was counseled about the need for surgery for definitive diagnosis.

### Treatment

The patient subsequently underwent an exploratory laparotomy and resection of all visible cyst areas. Intraoperatively, a large cystic lesion measuring  $10.4 \times 10.2 \times 14.1$  cm involving segments 8, 5, and 4b was found in the liver. The lesion extended into the porta hepatis and anteriorly over the pancreatic head and descending duodenum. After removal, the initial biopsy was consistent with a BCA. On gross examination, the lesion is cystic with multiple communicating lobules of varying sizes with a smooth and glistening lining. All areas of viable cyst were resected. Microscopic examination revealed a hepatobiliary cystadenoma without atypia or malignancy (Fig. 2).

She was followed for routine monitoring; however, an MRI 5 months later showed that there was still a cystic area in the liver bed where the initial resection of the cystadenoma occurred (Fig. 3). At the time it was unclear whether this was residual fluid collection from surgery, or recurrent BCA.

An MRI at 13 months postoperatively showed significant growth of the cyst, now measuring  $12 \times 9 \times 10$  cm, (previously  $9 \times 4 \times 7$  cm) and some mild intrahepatic biliary dilation (Fig. 4). During that visit, the patient reported pruritus, dark orange urine, and mustard-colored stools 2 weeks prior which had since resolved. The patient was again counseled about the need for surgical removal.

The patient was sent to gastroenterology for an ERCP where two 7-French stents were placed in the right and left bile ducts to facilitate surgical removal of the cyst. Extrinsic

compression of the common bile duct was noted as well.

Due to the patient's worsening symptoms and enlarging cyst on imaging, surgery was once again offered to the patient. Cystic resection was difficult due to the previous unroofing and enucleation of liver cyst where adhesions had developed. Complete resection of the cyst with formal central hepatectomy was performed. On the final pathology report, many sections showed cystic structures lined by cuboidal to columnar epithelial cells with bland, basally oriented nuclei, and an ovarian-type stroma with elongated and undulating nuclei underlying the epithelium. This was consistent with a multiloculated BCA, grossly measuring 10 cm in greatest dimension, with surgical margins negative for cystadenoma.

### Follow-up and outcomes

The patient did well postoperatively. Her most recent CT showed no recurrence of BCA, with evidence of central hepatectomy and compensatory hypertrophy (Fig. 5).

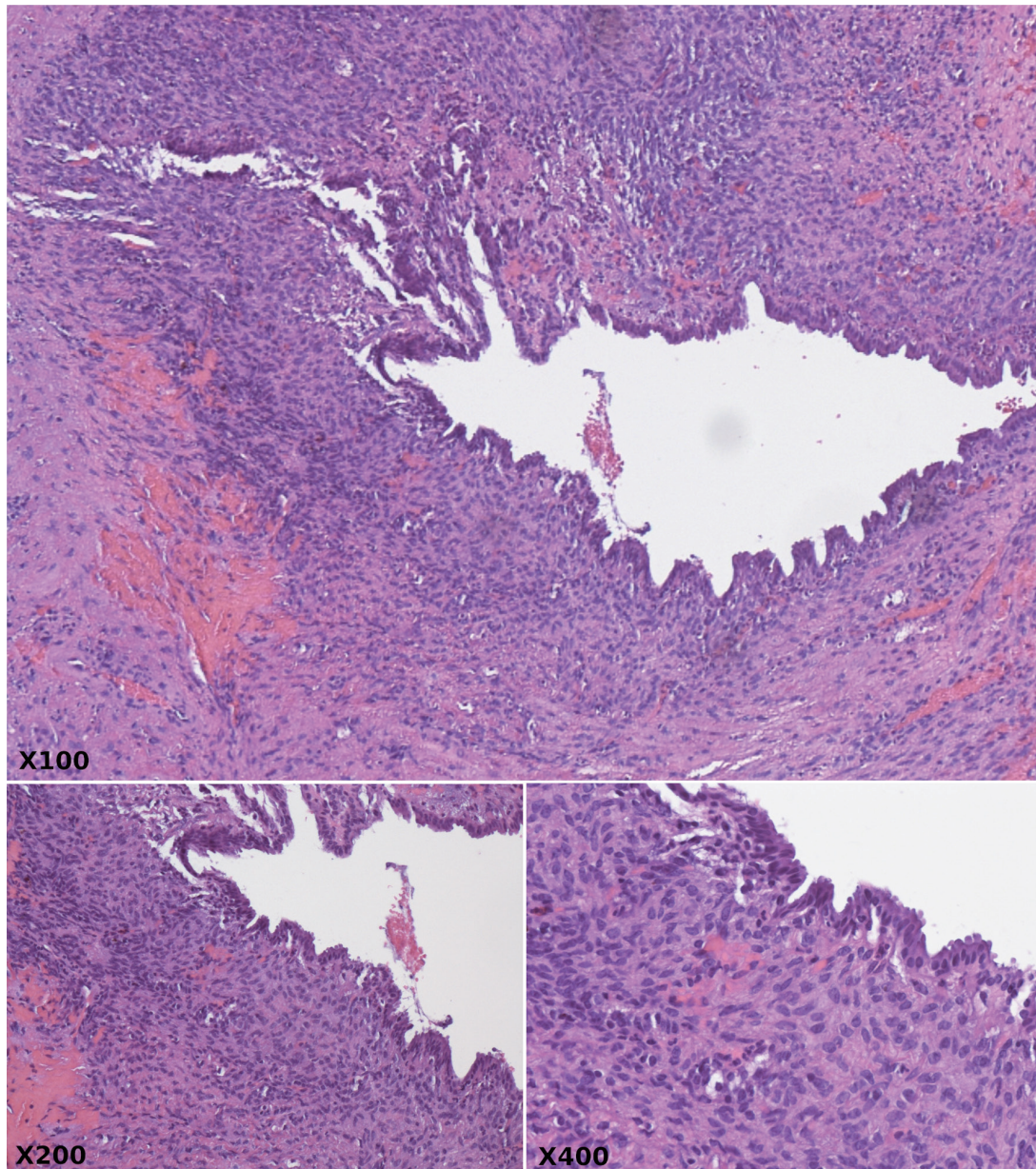
### Discussion

BCAs are rare, benign, tumors associated with the liver, and infrequently, the extrahepatic bile ducts. BCA and BCAC are tumors arising from the biliary epithelium. BCAs tend to occur in middle-aged women [2, 9-12] and have the potential for malignant transformation. This risk for transformation is thought to be as high as 20% to 30% [13]. Moreover, there have been a few case reports of benign cystadenomas transforming into cystadenocarcinomas [3, 14]. These instances further highlight their potential for malignant growth. While BCAs tend to occur more often in women, other studies have noted that BCACs tend to occur more in men [9, 10].

There is some discrepancy in the literature in terms of the prevalence of BCA. Most papers report an incidence of less than 5% of all hepatic cystic lesions [1, 2], but recent research estimates a lower incidence around 1.7% of intrahepatic cystic liver lesions [6]. Either way, these are rare tumors that should be considered when evaluating cystic lesions within the liver.

Most patients are asymptomatic at time of presentation and generally complain of vague abdominal symptoms [4-7]. One study reported that 88% of their patients with cystadenomas complained of upper abdominal pain or discomfort [11], while another stated that 74% of patients had abdominal pain [7]. Our patient presented with the usual complaints of abdominal pain and fullness. Interestingly, she also presented with the less often seen complaints of intermittent hyperbilirubinemia, dyspepsia, nausea, and vomiting. One study indicated that these rarer symptoms are likely due to pressure on adjacent viscera and organs [12] which would explain our patient's symptoms as she presented with a fairly large mass.

The differential diagnosis for our patient included a complex cyst, BCA/cystadenocarcinoma, complex biloma, or a possible lymphangioma. Other hepatic cyst differentials can be quite exhaustive and include degeneration of metastatic tu-



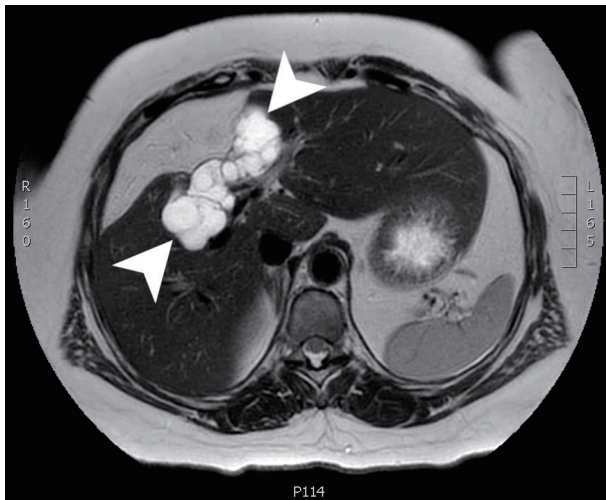
**Figure 2.** Hematoxylin and eosin stain at  $\times 100$ ,  $\times 200$ , and  $\times 400$  magnification revealing cystically dilated ducts lined by bland biliary columnar epithelium and surrounded by compact ovarian type spindle cell stroma.

mors, hematomas, parasitic disease, hamartomas, Caroli's disease, and polycystic liver disease [7, 15] to name a few.

Current diagnostic modalities highlight the difficulties in distinguishing biliary cystic tumors (BCT) from other hepatic lesions. Presently, there are no definitive, reliable clinical or imaging criterion for differentiating BCA from BCAC [15]. A clear example of this occurred in a study, where 16 patients were diagnosed preoperatively with BCA based on clinical and radiologic features, yet only six of these patients had BCA as their official diagnosis postoperatively [13]. Moreover, the non-specific imaging features of BCA make accurate preoperative diagnosis difficult [16]. Despite these limitations, there are some general imaging findings that can be extrapolated and used with

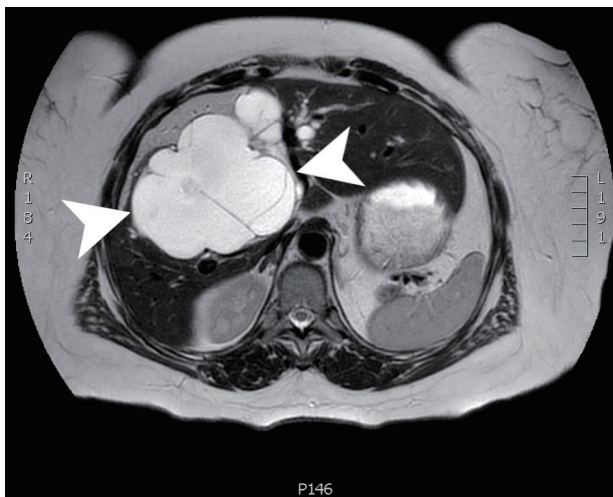
caution when a BCA is suspected. These include multilocular fluid collections with septations and debris on US [9], which was consistent with our patient's presentation. Further, imaging studies with CT and MRI of our patient again aligned with the literature showing multilocular cystic processes [17]. The only definitive method for differentiating BCA from BCAC is pathologic examination. Overall, further research is needed to improve preoperative diagnostic specificity, which would facilitate timely interventions and appropriate treatment.

Laboratory values, such as cystic fluid analysis (CFA), have been proposed to aid in diagnosis of BCA and to help differentiate from other hepatic lesions. One study found that CFA can differentiate between simple cysts and BCA, since BCA

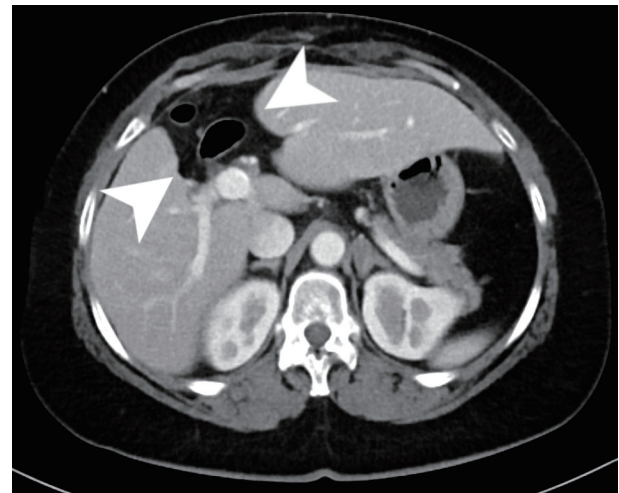


**Figure 3.** An axial slice from a T2 weighted MRI scan with Eovist (gadaxetate disodium) contrast. A multiloculated cystic mass (arrow heads) is seen involving the right hepatic lobe (segments 4 and 5) measuring  $8.0 \times 3.2 \times 3.2$  cm. MRI: magnetic resonance imaging.

exhibited elevated levels of carbohydrate antigen 19-9 (CA 19-9) while simple cysts had normal levels [18]. However, a different study found that cystic fluid CA 19-9 levels showed no significant difference between BCA and hepatic simple cysts [19]. Things get more difficult when differentiating between BCA and BCAC. One systematic review noted that liver function enzymes like aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) cannot be used to differentiate BCA from BCAC [20]. Furthermore, the same review found that elevated serum markers, like CA 19-9 and carcinoembryonic antigen (CEA), are suggestive of BCAC, but tumor markers within the normal range cannot rule out BCAC [20]. In general, further research is warranted in CFA, and blood markers, which might aid in differentiating



**Figure 4.** An axial slice from a T2 weighted MRI scan with Eovist contrast. A large, multiloculated cystic structure (arrow heads) within the central liver (segments 4, 5 and 8) measuring  $12.5 \times 8.9 \times 2.1$  cm. MRI: magnetic resonance imaging.



**Figure 5.** An axial slice from the venous phase of a CT scan with contrast. The scan shows chronic postoperative changes of a prior central hepatectomy within the inferior aspects of segments 4B and 8 (arrow heads) with evidence of compensatory hypertrophy of both the right and left hemi-liver. CT: computed tomography.

hepatic lesions in the future.

There is more agreement in terms of histology, where BCT seem to fall into one of two categories: those that contain mesenchymal (ovarian-like) stroma and those that do not [2]. In a study observing 22 patients with intrahepatic BCAs, the cyst lining consisted of biliary epithelium +/- mesenchymal stroma [18]. Moreover, another study noted that all the cystadenomas were multilocular with benign cuboidal to columnar epithelium, and 44 (85%) had densely cellular spindle cell (“ovarian-like”) stromata [2]. Similar findings were found in our patient who showed cystic structures lined by cuboidal to columnar epithelial cells with bland, basally oriented nuclei, and an ovarian-type stroma with elongated and undulating nuclei underlying the epithelium.

Complete surgical resection is the preferred treatment method for BCA to prevent recurrence and limit the potential for malignant transformation [5-7, 11, 13, 18, 21, 22]. One study found that recurrence following surgical resection of BCT was relatively high, with nearly one in five patients experiencing recurrence. They also noted that recurrence was considerably higher among patients who underwent unroofing/fenestrations compared to formal hepatic resection [9]. In comparison, a systematic review reported a recurrence of 5.4% after resection for BCA and 4.8% after resection for BCAC, while recurrence after fenestration or marsupialization varied from 81.6% to 100% for both BCA and BCAC [20]. Another study noted 39 patients with either BCA (n = 35) or BCAC (n = 4) who underwent resection and reported a recurrence rate of 2.6% [6]. Further, one study investigating 10 cases of BCA and BCAC found that there was no recurrence in all patients after a median follow-up of 6 years [23].

Overall survival and prognosis for BCA seem to be favorable. One study examined a large, multi-institutional cohort of patients with BCT, and noted an overall survival of 84.2% [9]. Moreover, another paper concluded that prognosis of BCA

and BCAC is excellent on most cases if a patient undergoes complete surgical resection [6]. Therefore, despite the potential for malignant transformation, complete resection yields favorable outcomes and prognosis for the patient.

Of note, current literature should be taken with a grain of salt, as most are single-center studies or based on a small sample size (often no more than 20 to 30 patients.) Therefore, future research on BCT is warranted.

## Conclusions

In conclusion, BCAs often present clinically with nonspecific and variable symptoms. They have the potential for malignant transformation and thus require further workup. The literature varies on the prevalence of recurrence in BCA and more research is needed. Current imaging modalities have yet to clearly identify ways to differentiate BCA from other cystic hepatic lesions. Complete surgical resection is the preferred method for the prevention or recurrence and the transformation of malignancy, which also confers a favorable outcome.

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None to declare.

## Financial Disclosure

None to declare.

## Conflict of Interest

None to declare.

## Informed Consent

Subject consent has been waived under the Institutional Review Board (IRB)-approved study protocol and the identity of the subject has been protected.

## Author Contributions

NB and MD: study design, data collection, literature review, manuscript writing, figures preparation, and review of final manuscript. HO, EC, PM, AB, WK and DRJ: Study design, literature review, manuscript writing, and review of final manuscript.

## Data Availability

Data supporting the findings of this study are available within the article.

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